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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,500	11/29/2000	David A Cheresh	TSRI 651.1	5356
2387	7590	04/19/2005	EXAMINER	
OLSON & HIERL, LTD. 20 NORTH WACKER DRIVE 36TH FLOOR CHICAGO, IL 60606			SCHNIZER, RICHARD A	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/701,500	CHERESH ET AL
	Examiner	Art Unit
	Richard Schnizer, Ph. D	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 02 February 2005.  
 2a) This action is FINAL. 2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,4,14-16,33 and 34 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1,4,14-16,33 and 34 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 29 November 2000 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_.  
 4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_.  
 5) Notice of Informal Patent Application (PTO-152)  
 6) Other: \_\_\_\_\_

## **DETAILED ACTION**

An amendment was received and entered on 2/2/05.

Claims 1, 4, 14-16, 33, and 34 are pending and under consideration in this Office Action.

### ***Specification***

The specification stands objected to. At page 4 the brief description of Fig. 7 describes Figures 7A and 7B, however, Fig. 7 does not contain Figures 7A and 7B. Applicant has not responded to this objection.

### ***Claim Objections***

Applicant's amendment was sufficient to overcome the previous objection to claim 16.

### ***Rejections Withdrawn***

The rejection of claims 1, 4, 14-16, 33, and 34 for new matter is withdrawn in view of Applicant's amendments.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 16 stand rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al (FEBS Lett. 411:317-321, 1997), as evidenced by the instruction manual for the BioRad Gene Pulser, retrieved on 10/15/2004 from <http://researchlink.labvelocity.com/protocols/protocol.jhtml?sourceld=25&path=0%7C669%7C1014%7C848&nodeld=848&id=2121>.

Kato teaches a non-viral vector (pOPI3) comprising a human c-Src cDNA, and the use of the vector to transfect NIH 3T3 cells by electroporation using a BioRad Gene Pulser apparatus. As is apparent to one of ordinary skill in the art, in order to work with nucleic acid compositions, the compositions must be contained somehow, e.g. in a vial, a microfuge tube, a pipette tip, or even an electroporation cuvette. The operating instructions for the electroporation apparatus used by Kato show that the electroporation process involves placing the nucleic acid composition into an article of manufacture, i.e. an electroporation cuvette. See e.g. page 12, item 4. It is clear that the nucleic acid of Kato was in a carrier/excipient i.e. water, because the electroporation procedure is carried out with nucleic acids in a cell suspension. See e.g. page 12, item 4, or page 14, last full paragraph of the instruction manual.

It is noted that, in order to be enabled, the claimed nucleic acid must be capable of stimulating angiogenesis in a tissue to which it is directly applied. The instant specification provides no guidance as to what is the minimum amount of the nucleic acid which is required to stimulate angiogenesis. Because the claimed nucleic acid and the nucleic acid of Kato are structurally indistinguishable, the nucleic acid of Kato is

considered to be capable of stimulating angiogenesis to a tissue in which it is directly applied, and to be able to produce the required amount of protein, absent evidence to the contrary. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best*, *Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus Kato anticipates the claims.

Claims 1, 4, and 15 stand rejected under 35 U.S.C. 102(b) as being anticipated by Tanaka et al (Mol. Cell. Biol. 6(11): 3900-3909, 1986).

Tanaka teaches isolation of a retroviral vector (WO CS) encoding a human c-src protein. See entire document, especially abstract. It is readily apparent to one of ordinary skill in the art, in order to isolate virus vectors, the vectors must be contained somehow, in an article of manufacture, e.g. in a vial, or microfuge tube. Thus Tanaka anticipates the claims.

***Response to Arguments***

Applicants arguments filed 2/2/05 have been considered as they may apply to the grounds of rejection set forth above, but are unpersuasive.

Applicant addresses the anticipation rejections at pages 5-8 of the response. Applicant notes at page 5 that claims 1, 4, and 16 are drawn to articles of manufacture, and argues that the cited art does not teach an article of manufacture comprising packaging material. This is unpersuasive because it is clear that one cannot work with nucleic acids or virus vectors in the manner disclosed in the cited art without the aid of packaging materials such as vials, microfuge tubes, pipette tips or electroporation cuvettes that are used to contain the nucleic acids or viral vectors. Further, as discussed more fully below, the claimed nucleic acid is the functional element of the invention, and the recited packaging material is not functionally related to the recited nucleic acid. The packaging material in no way affects the structure or function of the nucleic acid. As a result, the packaging material will not distinguish the claimed nucleic acid from the nucleic acid of the prior art.

At pages 5-7 of the response, Applicant argues the significance of printed words on a label. Applicant argues that the facts of *In re Ngai*, relied upon by the Office to support the rejection, are distinguishable from those of the instant case. However, Applicant's argument is essentially the same as that set forth previously, i.e. the printed matter on the label should be given patentable weight because the instructions and information on the label impart specific, new functionality to the article of manufacture

that was previously unknown to one of ordinary skill in the art. Applicant argues that this situation is analogous to that set forth in *In re Gulack* and *In re Miller*.

This argument regarding *Gulack* and *Miller* is unpersuasive for the reasons of record, i.e. because the situations are not analogous. The functional element of the instant invention is the nucleic acid that encodes the human src protein and can stimulate angiogenesis. The packaging material cannot stimulate angiogenesis. The label cannot stimulate angiogenesis. The situations are not analogous because neither the packaging material nor the printed instructions change the functionality or impart a new functionality to the nucleic acid. The nucleic acid still encodes the same protein known in the prior art, and the protein still catalyzes the same kinase reaction known in the prior art. The activity of this kinase is required for the stimulation of angiogenesis. The presence of packaging material or instructions changes nothing with regard to the intrinsic function of the nucleic acid. In contrast, in both *Gulack* and *Miller*, the printed matter changed the intrinsic qualities of the material to which it was applied. In other words, the functions of the claimed devices depended on the printed matter itself, which was part of the substrate. That is, the printed matter was part of the hat in *Gulack*, and part of the cup in *Miller*, and in each case the printed matter altered both the structure and the function of the material to which it was applied. In both cases, without the printed material, the substrates lose their distinguishing function. In the instant case, the printed matter is merely a label that indicates that the claimed nucleic acid may be used for a particular purpose, but the label itself does not change the structure of the claimed nucleic acid or confer any new or different functionality on the claimed nucleic

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acid. In fact, the nucleic acid retains its full functionality absent the recited printed material.

Applicant argues that *Ngai* is distinguishable from the instant case because in *Ngai*, the cited art taught printed material (a set of instructions), whereas the currently cited art does not. Applicant argues that the printed matter on the label should be given patentable weight because the instructions and information on the label impart specific, new functionality to the article of manufacture that was previously unknown to one of ordinary skill in the art. This argument is unpersuasive because the court found in the *Gulack* and *Ngai* decisions that , “[w]here the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability.” The label in this case carries no patentable weight because it is not functionally related to the substrate, i.e. it does not affect the intrinsic function of the nucleic acid in any way, as discussed above. As in *Ngai*, all the printer matter does is teach a new use for an existing product. If the labels such as that claimed instantly were given patentable weight, then anyone could continue patenting a product indefinitely provided that they add a new label to the product. In *Ngai*, the court stated that this was not envisioned by *Gulack*. In this application, neither the packaging material nor the printed matter is functionally related to the nucleic acid, so neither one will patentably distinguish the invention from the nucleic acid of the prior art. For these reasons the rejections are maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 14, and 15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al (FEBS Lett. 411:317-321, 1997), in view of Boyse et al (US Patent 5,004,861, issued 4/2/1991).

Kato teaches a method in which expression vectors comprising a human c-Src cDNA are used to stably transfet cultured cells for the purpose of studying cellular metabolism. The cells were transfected by electroporation.

Kato does not teach a liposome or a viral vector.

Boyse teaches methods of making stably transfected cells with genes. At paragraph 148 of the detailed description, Boyse notes that numerous techniques are known in the art for the stable introduction of foreign genes into cells, and further states:

Techniques which may be used include but are not limited to chromosome transfer (e.g., cell fusion, chromosome-mediated gene transfer, micro cell-mediated gene transfer), physical methods (e.g., transfection, spheroplast fusion, microinjection, electroporation, liposome carrier), viral vector transfer (e.g., recombinant DNA viruses, recombinant RNA viruses) etc. [citation omitted].

Thus Boyse teaches that electroporation, liposome-mediated transfection, and virus-mediated transfection are interchangeable for the purpose of delivering genes to cells. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one

equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). For these reasons it would have been obvious to one of ordinary skill in the art at the time of the invention to use liposomes to transfer into cells the human c-src expression vector of Kato. Similarly, it would have been obvious to construct and use a viral vector comprising the human c-Src cDNA. Regarding the claimed packaging material, it is readily apparent to one of ordinary skill in the art that in order to work with nucleic acid compositions, the compositions must be contained somehow, e.g. in a vial, a microfuge tube, or a pipette tip. As such the presence of a packaging material is considered to be obvious, and the invention as a whole was *prima facie* obvious.

It is noted that, in order to be enabled, the claimed composition must be capable of stimulating angiogenesis in a tissue to which it is directly applied. The instant specification provides no guidance as to what is the minimum amount of the composition which is required to stimulate angiogenesis. Because the claimed pharmaceutical composition and the composition of Kato are structurally indistinguishable, the composition of Kato is considered to be capable of stimulating angiogenesis to a tissue in which it is directly applied, and to be able to produce the required amount of protein, absent evidence to the contrary. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971).

Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 33 and 34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al (FEBS Lett. 411:317-321, 1997), in view of Boyse et al (US Patent 5,004,681, issued 4/2/1991) and GenBank Accession No. X59932.

The teachings of Boyse and Kato are summarized above, and render obvious compositions comprising a human c-Src expression vector associated with liposomes, and a viral expression vector encoding human c-Src.

Kato is silent as to the sequence of the human c-src encoded by the cDNA. GenBank Accession No. X59932 teaches a nucleic acid encoding a human c-Src polypeptide having the sequence of SEQ ID NO:5.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use in the invention of Kato the c-Src sequence disclosed in GenBank Accession No. X59932. The essential feature of the cDNA of Kato is that it encoded a human c-SRC with kinase activity. The nucleic acid of GenBank Accession No. X59932 encodes a human c-Src kinase. As such, these nucleic acids would be considered by those of ordinary skill in the art to be interchangeable in the invention of

Kato, and so they are equivalents. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of *prima facie* obviousness. See also *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945).

It is noted that, in order to be enabled, the claimed composition must be capable of stimulating angiogenesis in a tissue to which it is directly applied. The instant specification provides no guidance as to what is the minimum amount of the composition which is required to stimulate angiogenesis. Because the claimed pharmaceutical composition and the composition of Kato are structurally indistinguishable, the composition of Kato is considered to be capable of stimulating angiogenesis to a tissue in which it is directly applied, and to be able to produce the required amount of protein, absent evidence to the contrary. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie

obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus the invention as a whole was *prima facie* obvious.

### ***Response to Arguments***

Applicants arguments filed 2/2/05 have been considered as they may apply to the grounds of rejection set forth above, but are unpersuasive.

Applicant argues at pages 7 and 8 of the response that Kato does not teach several limitations of the claims, as discussed in the response to the rejections under 35 USC 102, and that the secondary references also fail to teach these limitations. Applicant's arguments regarding the Kato reference are unpersuasive for the reasons given above under 35 USC 102 rejections. Applicant has not argued that the secondary references do not teach the limitations for which they were relied upon. For these reasons the rejections are maintained.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.

ANNE M. WEHBE, PH.D  
PRIMARY EXAMINER

